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Spontaneous assembly of bivalent single chain antibody fragments in Escherichia coli.

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The ability of immunoglobulin Fab and single chain (ScFv) fragments to penetrate effectively into tissue from the vascular system has made these molecules excellent candidates as drug delivery systems and imaging tools. This study investigates the use of single chain antibody fragment bacterial expression vectors as a possible strategy for the production of these molecules. We have modified the pSW1-VHD1.3-VKD1.3-TAG1 vector [Ward et al. (1989) Nature 341, 544-546] which originally, when expressed in E. coli, produced an Fab fragment. In an effort to improve the affinity of the parent vector product a novel single chain antibody construct which encodes a protein with anti-P. aeruginosa activity was generated using a 14 amino acid linker [Chaudhary et al. (1990) Proc. natn. Acad. Sci. U.S.A. 87, 1066-1070]. In addition to the heavy and light chain variable domain genes, our construct also contained the light chain kappa constant domain gene to aid purification of the fragments. To underline this difference from the conventional ScFv fragment we have described this protein as a ScAb. The ScAb generated had an antigen binding capacity similar to the parent anti-P. aeruginosa antibody but was superior to the recombinant anti-P. aeruginosa Fab fragment. On HPLC and non-denaturing gel electrophoresis analysis, the ScAb was found to exist in multimeric forms while the Fab fragment existed only as a single unit. Dimeric ScAb had a similar antigen binding profile to the parent antibody.

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